Specification Amendments

Please amend the specification as follows:

Please amend the **paragraph on page 26, lines 4-13** as follows:

The fluid dispensing device normally includes a reagent source or manifold as well as reagent lines that connect the source to fluid dispensing nozzles and the like. Any system may be employed that dispenses fluids such as water, aqueous media, organic solvents and the like. The fluid dispensing device may comprise ~~comprises~~ a pump for moving fluid and may also comprise a valve assembly and a manifold as well as a means for delivering predetermined quantities of fluid to the surface of a support. The fluids may be dispensed by any of the known techniques such as those mentioned above. Any standard pumping technique for pumping fluids may be employed in the dispensing device. For example, pumping may be by means of a peristaltic pump, a pressurized fluid bed, a positive displacement pump, e.g., a syringe pump, and the like.

Claim Amendments

Please amend the claims as follows:

Claims 1-37 (canceled)

38. (currently amended) A method for forming a chamber having a controllable interior environment for preparing an array of biopolymers on the surface of a support, said method comprising:

(a) disposing a separate top element and a separate bottom element relative to one another to form a gap therebetween, and

(b) introducing a gas into said gap, a ~~the~~ pressure of said gas being sufficient to form an ~~a movable~~ aerodynamic seal between said top element and said bottom element thereby forming said chamber wherein said top element or said bottom element is movable with respect to the other during said aerodynamic seal.

39. (currently amended) A method according to Claim 38 wherein said gas is introduced adjacent a ~~the~~ perimeter of said top element and a ~~the~~ perimeter of said bottom element.

40. (original) A method according to Claim 38 wherein said bottom element comprises side walls and said gas is introduced through openings in said side walls of said bottom element.

41. (currently amended) A method according to Claim 40 wherein said gas is introduced ~~into~~ at a pressure of about 20 to about 50 psi.

42. (original) A method according to Claim 40 comprising introducing a second gas into the interior of said chamber after step (b).

43. (currently amended) A method according to Claim 42 wherein a ~~the~~ flow of said second gas through the interior of said chamber is substantially uniform.

44. (currently amended) A method according to Claim 42 wherein a ~~the~~ flow of said second gas within the interior of said chamber is dispersed.

45. (currently amended) A method according to Claim 42 wherein a ~~the~~ flow of said second gas is dispersed as it enters said chamber.

46. (original) A method according to Claim 42 wherein said second gas is selected from the group consisting of nitrogen, argon, neon and helium.

47. (currently amended) A method according to Claim 38 wherein said gas is introduced into an ~~the~~ interior of said chamber and flows outwardly therefrom through said gap.

48. (currently amended) A method for synthesizing an array of biopolymers on a support, said method comprising:

(a) performing a step in the synthesis of an array of biopolymers on a support in ~~forming~~ a reaction chamber formed between ~~by disposing~~ two elements disposed relative to one another in a sealed, movable relationship, wherein

~~(b) bringing said support within said reaction chamber to perform a step in the synthesis of said array on said support wherein~~ said support and one of said elements is moved relative to the other of said elements during said performing,

(be) removing said support from said reaction chamber, and

(c~~d~~) optionally repeating steps (a~~b~~) through (b~~d~~) until said array of biopolymers ~~biopolymer~~ is formed.

49. (currently amended) A method according to Claim 48 wherein said reaction chamber is formed by disposing two elements relative to one another to form a gap therebetween~~,~~ and introducing a gas into said gap to form a sealed reaction chamber comprising said two elements.~~,~~

50. (currently amended) A method for synthesizing an array of biopolymers on a support, said method comprising:

(a) introducing a support into ~~forming~~ a reaction chamber formed between ~~by disposing~~ a separate top element and a separate bottom element disposed relative to one another to form a gap therebetween, said ~~a~~ top element having sealingly affixed therein at least a portion of a device for dispensing reagents, said bottom element being adapted for introduction of a support therethrough, wherein ~~and introducing~~ a gas is introduced into said

gap, a ~~the~~ pressure of said gas being sufficient to form an ~~a movable~~ aerodynamic seal between said top element and said bottom element thereby forming said chamber, and wherein said top element or said bottom element is movable with respect to the other during said aerodynamic seal

(b) ~~introducing said support into said reaction chamber, said support being activated,~~

~~(c)~~ bringing said support and a dispensing system for dispensing reagents for the synthesis of said biopolymers into a dispensing position relative to discrete sites on said ~~activated~~ surface of said support by moving said support and said bottom element relative to said top element,

(c) activating said support if said support is not already activated and dispensing said reagents to said discrete sites to perform a step of said synthesis,

(d) removing said support and/or said dispensing system from said relative dispensing position, and

(e) optionally repeating steps (a~~b~~) through (d) until said array of biopolymers ~~biopolymer~~ is formed.

51. (currently amended) A method according to Claim 50 wherein said gas is introduced adjacent a ~~the~~ perimeter of said top element and a ~~the~~ perimeter of said bottom element.

52. (original) A method according to Claim 50 wherein said gas is introduced through openings in side walls of said bottom element.

53. (currently amended) A method according to Claim 50 wherein said gas is introduced ~~into~~ at a pressure of about 20 to about 50 psi.

54. (currently amended) A method according to Claim 50 comprising introducing a second gas into an ~~the~~ interior of said chamber after step (b).

55. (currently amended) A method according to Claim 54 wherein a ~~the~~ flow of said second gas through the interior of said chamber is substantially uniform.

56. (currently amended) A method according to Claim 54 wherein a ~~the~~ flow of said second gas within the interior of said chamber is dispersed.

57. (original) A method according to Claim 54 wherein said second gas is selected from the group consisting of nitrogen, argon, neon and helium.

58. (original) A method according to Claim 50 wherein said reagents are monomer addition reagents.

59. (original) A method according to Claim 50 wherein an array of said biopolymers is synthesized on said support.

60. (original) A method according to Claim 50 wherein said biopolymers are polynucleotides or polypeptides.

61. (original) A method according to Claim 50 wherein said biopolymers are synthesized on said surface in multiple arrays and said support is subsequently diced into individual arrays of biopolymers on a support.

62. (currently amended) A method according to Claim 50 for synthesizing an array of biopolymers on a surface of a support, said method comprising adding one or more polymer subunits at each of multiple feature locations on said support during each of multiple rounds of subunit additions wherein each round of subunit additions comprises:

(a) introducing said support into said reaction chamber,

(b) bringing said support and a dispensing system for dispensing said polymer subunits for the synthesis of said biopolymers into a dispensing position relative to said ~~activated~~ discrete sites on said surface,

(c) dispensing said polymer subunits to said discrete sites, and

(d) removing said support and/or said dispensing system from said ~~relative~~ dispensing position.

63. (original) A method according to Claim 50 wherein said biopolymers are synthesized on said surface in multiple arrays and said support is subsequently diced into individual arrays of biopolymers on a support.

64. (original) A method according to claim 50 further comprising exposing the array to a sample and reading the array.

65. (original) A method according to claim 64 comprising forwarding data representing a result obtained from a reading of the array.

66. (original) A method according to claim 65 wherein the data is transmitted to a remote location.

67. (original) A method according to claim 64 comprising receiving data representing a result of an interrogation obtained by the reading of the array.

68. (new) A method according to Claim 50 wherein said top element is stationary and said bottom element is moved relative to said top element to bring said support and said dispensing system for dispensing reagents for the synthesis of said biopolymers into a dispensing position relative to discrete sites on said surface of said support.

REMARKS

Applicant requests reconsideration of the present application in view of the foregoing amendments and the discussion that follows. The status of the claims is as follows. Claims 1-67 are pending. The Examiner has withdrawn claims 1-37 from consideration and such claims have been canceled herein without prejudice to Applicant's filing of divisional applications to the separately patentable subject matter thereof. Claims 38, 39, 41, 43-45, 47-51, 53-56 and 62 have been amended herein and Claim 68 has been added.

The Amendment

The Specification was amended to correct an obvious typographical error.

Claim 1 was amended to recite that the top element or the bottom element is movable with respect to the other during the aerodynamic seal. Support therefor is in the Specification, for example, page 8, lines 6-8. Claim 1 was also amended to provide proper antecedent basis as kindly suggested by the Examiner.

Claims 39, 43-45, 47, 51 and 54-56 were amended to provide proper antecedent basis as kindly suggested by the Examiner.

Claim 41 was amended to correct a typographical error.

Claim 45 was also amended to recite that the said second gas is dispersed as it enters said chamber. Support therefor is in the Specification, for example, original Claim 11.

Claim 48 was amended to recite "performing a step in the synthesis of an array of biopolymers on a support in a reaction chamber formed between two elements disposed relative to one another in a sealed, movable relationship, wherein said support and one of said elements is moved relative to the other of said elements during said performing." Support therefor is in the Specification, for example, original Claim 48. Claim 48 was also amended to recite that the steps are repeated until said array of biopolymers is formed. Support therefor is in the Specification, for example, original Claim 48.

Claim 49 was amended to correct obvious punctuation errors.

Claim 50 was amended to recite for step (a) "introducing a support into a reaction chamber formed between a separate top element and a separate bottom element disposed relative to one another to form a gap therebetween, said top element having sealingly affixed therein at least a portion of a device for dispensing

reagents, said bottom element being adapted for introduction of a support therethrough, wherein a gas is introduced into said gap, a pressure of said gas being sufficient to form an aerodynamic seal between said top element and said bottom element thereby forming said chamber." Support therefor is in the Specification, for example, original Claim 50, steps (a) and (b). Claim 50 was also amended in step (a) to recite that the top element or the bottom element is movable with respect to the other during the aerodynamic seal. Support therefor is in the Specification, for example, page 8, lines 6-8. Claim 50 was also amended to provide proper antecedent basis as kindly suggested by the Examiner. Claim 50 was also amended to recite the step of activating the support if the support is not already activated. Support therefor is in the Specification, for example, original Claim 50. Claim 50 was also amended in step (c) to recite that reagents are dispensed to discrete sites to perform a step of the synthesis. Support therefor is in the Specification, for example, original Claim 50. Claim 50 was also amended to recite that the steps are repeated until said array of biopolymers is formed. Support therefor is in the Specification, for example, original Claim 50.

Claim 53 was amended to correct a typographical error.

Claim 62 was amended to delete "activated" in step (b) and "relative" in step (d).

Claim 68 was added and finds support in the specification, for example, page 8, lines 23-25.

Oath/Declaration

Applicant filed a declaration in which page 2 thereof was executed in counterparts so that the total number of pages was 3. One page 2 of the declaration was executed by the inventors except for Maryam Mobed-Miremadi. The other page 2 was executed by the latter.

On September 8, 2003, the Examiner confirmed the above and indicated that the originally filed declaration was not defective as set forth in the Office Action. Applicant regrets the confusion caused by the counterpart page 2's of the original declaration.

Objection to the Drawings

Formal drawings are being submitted herewith. It is believed that the formal drawings obviate the objection to the drawings set forth in the Office Action.

Discussion of Certain Aspects of the Invention

Applicant first would like to discuss certain aspects of the present invention prior to addressing the rejections in the Office Action in order to avoid any misunderstanding concerning aspects of the present methods.

As explained in Applicant's Specification, in one aspect the present invention provides a method for forming a reaction chamber wherein one portion of the chamber may be moved relative to another portion by means of a movable aerodynamic seal. One of the portions may comprise, for example, a device for dispensing reagents and the other portion may comprise, for example, a holder for a support on the surface of which chemical compounds are synthesized. In this way the volume of the reaction chamber may be kept as small as possible thereby making control of the environment inside the reaction chamber easier. One portion of the reaction chamber may be moved by appropriate motion stages while the other portion remains stationary. The two portions are separated by a gap, into which gas is directed to provide a movable aerodynamic seal. Because of the relatively small volume of the chamber, the desired level of humidity and other atmospheric conditions within the chamber are achieved more quickly than with relatively larger chambers. The gap between the two portions is positioned such that a chamber having a movable aerodynamic seal is formed, which allows one of the portions to be moved relative to other portion. The position of the gap determines the size of the chamber. The gap may be positioned at or near the perimeter of one of the portions and gas may be introduced into the gap from an area at or near the perimeter of the portion. The methods of the invention have particular application to the deposition or *in situ* synthesis of arrays of biopolymers where a substrate surface is moved relative to a reagent dispensing device to deposit droplets of reagents at sites on the surface of the substrate. Such synthesis involves multiple cycles of such deposition.

Rejection under 35 U.S.C. §112

Applicant believes that the above amendments obviate the rejections set forth in the Office Action. With regard to the rejection of Claims 38-47 as indefinite

in Claim 38, step b, or Claims 50-67 in step a, for the recitation "to form a movable aerodynamic seal," Applicant submits that the seal is both aerodynamic and movable as clearly taught in the specification. The seal is aerodynamic because it is formed by introducing gas into a gap where the motion of the gas forms the seal. The seal is movable because portions of the device may be moved relative to one another during the aerodynamic seal. See the Specification, for example, page 8, lines 6-8, 23-26, and page 11, lines 29-31.

Rejection under 35 U.S.C. §102

Claims 38, 39, 47-51, 58-60, 62 and 64 were rejected under 35 U.S.C. 102(b) as being anticipated by Winkler, *et al.* (U.S. Patent No. 5,677,195) (Winkler) as defined by Webster's Ninth New Dictionary (Merriam Webster Inc., Springfield MA, 1991, page 60).

In order to maintain a rejection under 35 U.S.C. §102(b), the Examiner must first establish a *prima facie* case of anticipation. An invention is anticipated if each and every limitation of the claimed invention is disclosed in a single prior art reference. *In re Paulsen*, 30 F.3d 1475, 1478, 31 U.S.P.Q.2d 1671, 1673 (Fed. Cir. 1994). In the present situation WInkler does not disclose each and every element of the claimed invention. Winkler fails to disclose or suggest a movable aerodynamic seal. Winkler fails to disclose a gap into which air is introduced wherein the motion of the air forms a movable aerodynamic seal. Winkler teaches only introducing pressurized gas into a chamber to immobilize a substrate while fluids are flowed through a channel. There is no movable aerodynamic seal. As a matter of fact, Winkler teaches that the upper and lower portions of the pressure chamber housing are held together by nuts and bolts and suggests other means such as clamps to hold the housing together. See, for example, column 12, lines 18-22. There is nothing movable with respect to the portions of Winkler's device during a seal.

The Examiner has interpreted the phrase "movable aerodynamic seal" to mean movement of air to form a seal. However, such an interpretation completely overlooks the word "movable" because, as the Examiner has realized, "aerodynamic" means motion of air. Whether "movable" modifies "aerodynamic" or "seal" is clear from Applicant's Specification. The recitation "movable aerodynamic" is not redundant because the phrase is "movable aerodynamic seal" not "movable

aerodynamic." The Examiner stated that, if "movable" is intended to modify "seal", this implies that the seal is moved from one location to another in which case it is unclear whether a seal is formed between the top and bottom elements. In the present invention as seen in the Specification, the seal is moved from one location to another during the seal. This allows the portions of the device to be moved relative to one another, thereby resulting in a much smaller reaction chamber than could otherwise be realized absent the "movable aerodynamic seal."

Regarding Claim 39, Winker does not disclose or suggest a method wherein gas is introduced adjacent the perimeter of top and bottom elements to form a movable aerodynamic seal.

Regarding Claim 47 and the introduction of a second gas into the reaction chamber formed by the movable aerodynamic seal, Applicant indicated in the Specification that it is usually the practice in the art to introduce a gas into the interior of reaction chambers to provide for a desired atmospheric condition within the interior of the chamber such as, for example, a desired atmosphere, a desired level of humidity, and the like. Such a teaching has no relevance to the movable aerodynamic seal of the present invention.

Regarding Claim 48, the Examiner contends that Winkler discloses a method for synthesizing an array of biopolymers on a support comprising forming a reaction chamber by disposing two elements relative to one another in a moveable relationship, binding said support into the reaction chamber to perform a step of synthesis and removing the support from the chamber. As discussed above, Winkler teaches that the upper and lower portions of the pressure chamber housing are held together by nuts and bolts and suggests other means such as clamps to hold the housing together. There is nothing movable about the portions of Winkler's device during an aerodynamic seal.

Regarding Claim 49, Winkler does not disclose or suggest a method wherein a reaction chamber is formed by disposing two elements relative to one another to form a gap and introducing a gas into the gap to form a sealed reaction chamber comprising the two elements where the two elements are movable with respect to one another during the seal.

For the reasons discussed above with respect to Claim 38 and claims dependent thereon, Winkler does not disclose or suggest the methods of Claims 50, 51, 58, 59, 60, 62 and 64.

Claims 38, 39 and 47 were rejected under 35 U.S.C. 102(a) and (b) as being anticipated by Schembri, *et al.* (U.S. Patent No. 6,258,593) (Schembri) as defined by Webster's Ninth New Dictionary (Merriam Webster Inc., Springfield MA, 1991, page 60).

Schembri does not disclose each and every element of the claimed invention. Schembri does not disclose or suggest a movable aerodynamic seal. Schembri does not disclose a gap into which air is introduced wherein the motion of the air forms a movable aerodynamic seal. Schembri teaches introducing an air bubble into a reaction chamber together with reaction fluid. The chamber is moved by rotation or nutation (column 12, lines 1-2) to create movement of the bubble within the fluid to achieve mixing. There is no movable aerodynamic seal. As a matter of fact, Schembri teaches that the upper and lower portions of the pressure chamber housing are held together by screws or clamps or springs or weights with an optional but preferred gasket or the like between the two portions to improve the seal. See, for example, column 8, lines 24-34, and column 10, line 64, to column 11, line 41. There is nothing movable about the portions of Schembri's apparatus during a seal.

Regarding Claim 39, Schembri does not disclose or suggest a method wherein gas is introduced adjacent the perimeter of top and bottom elements to form a movable aerodynamic seal.

The Examiner included a rejection of Claim 40 under this section although Claim 40 was not specifically mentioned in the introductory paragraph. Regarding Claim 40, Schembri does not disclose or suggest a method wherein gas is introduced adjacent the perimeter of top and bottom elements to form a movable aerodynamic seal.

Regarding Claim 47, Schembri does not disclose or suggest a method wherein gas is introduced adjacent the perimeter of top and bottom elements to form a movable aerodynamic seal.

Rejection under 35 U.S.C. §103

Claims 40, 42-46, 52 and 54-57 were rejected under 35 U.S.C. 103(a) as being unpatentable over Winkler as defined by Webster's Ninth New Dictionary (Merriam Webster Inc., Springfield MA, 1991, page 60) in view of Schembri.

In order to maintain a rejection under 35 U.S.C. §103 the Examiner must first establish a *prima facie* case of obviousness. *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988); *In re Piasecki*, 745 F.2d 1468, 223 U.S.P.Q. 785 (Fed. Cir. 1984). In determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the references before him to make the proposed substitution, combination or other modification. *In re Lintner*, 458 F.2d 1013, 173 U.S.P.Q. 560 (C.C.P.A. 1972). In determining the scope and content of the prior art, references must be considered in their entirety, as a whole, including portions that would lead away from the claimed invention. *In re Panduit*, 810 F.2d 1561, 1 U.S.P.Q.2d 1593 (Fed Cir. 1987). Hindsight reconstruction using the disclosure and claims in prosecution as a guide to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention is not permitted. *In re Fine*, *supra*.

Regarding Claims 40 and 42-45, the Examiner argues that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the gas introduction of Winkler introducing gas into the chamber via the bottom element whereby the gas bubbles are dispersed within the chamber to thereby facilitate mixing within the chamber as taught by Schembri. The teachings of Winkler and Schembri are deficient, among others, in making no disclosure or suggestion of a movable aerodynamic seal as discussed above in the rejection under 35 U.S.C. 102. The combined teachings of the references do not overcome these deficiencies.

The above rationale applies as well to the rejection of Claim 46 under the above code section.

Regarding Claim 52 and 54-56, the Examiner argues that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the gas introduction of Winkler by introducing gas into the chamber via the bottom element whereby the gas bubbles are dispersed within the chamber to thereby facilitate mixing within the chamber as taught by Schembri. The teachings of Winkler and Schembri are deficient, among others, in making no disclosure or suggestion of a movable aerodynamic seal as discussed above in the rejection under 35 U.S.C. 102. The combined teachings of the references do not overcome these deficiencies.

The above rationale applies as well to the rejection of Claim 57 under the above code section.

Claims 41 and 53 were rejected under 35 U.S.C. 103(a) as being unpatentable over Winkler as defined by Webster's Ninth New Dictionary in view of Schembri as applied to Claims 40 and 50 above and further in view of Anderson, *et al.* (U.S. Patent No. 6,168,948) (Anderson).

Regarding Claims 41 and 53, the Examiner asserts that Winkler and Schembri teach the methods of Claims 40 and 50 as discussed above wherein a gas is introduce into a reaction chamber and that Anderson teaches a similar method wherein gas introduced into the chamber for sealing the chamber is about 20 to about 50 psi. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made, concludes the Examiner, to apply a pressure of about 20 to about 50 psi to the gas introduced by Winkler and Schembri based on the teaching of Anderson wherein the claimed pressure is useful as a sealing pressure (Example 6, Column 67, lines 34-36).

As discussed above, the teachings of Winkler and Schembri are deficient, among others, in making no disclosure or suggestion of a movable aerodynamic seal. The combined teachings of the references do not overcome these deficiencies. At column 67, lines 34-36, Anderson teaches only that elastomeric valves were opened and closed by application of vacuum or pressure (approx. 60 psi) to the space above the individual valves.

Claims 61 and 63 were rejected under 35 U.S.C. 103(a) as being unpatentable over Winkler as defined by Webster's Ninth New Dictionary in view of Besemer, *et al.* (U.S. Patent No. 6,399,362). (Besemer)

Regarding Claims 61 and 63, the Examiner argues that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the multiple array synthesis of Besemer to the array synthesis of Winkler to thereby provide a plurality of identical arrays on a single surface as taught by Besemer (Column 6, lines 25-36).

As discussed above, the teachings of Winkler are deficient, among others, in making no disclosure or suggestion of a movable aerodynamic seal. The teaching of Besemer, when combined with Winkler, does not overcome these deficiencies.

Claims 65-67 were rejected under 35 U.S.C. 103(a) as being unpatentable over Winkler as defined by Webster's Ninth New Dictionary in view of Abraham-

Fuchs, *et al.* (U.S. Patent No. 6,484,104) (Abraham-Fuchs). The heading to this section in the Office Action indicates that the rejection is under U.S.C. § 103 over Winkler in view of Besemer. However, as indicated above, the rejection in the body of the text was made over Winkler in view of Abraham-Fuchs. Applicant assumes the heading to be a typographical error and addresses below the rejection as over Winkler in view of Abraham-Fuchs. If Applicant's assumption is incorrect, Applicant respectfully requests that Applicant be given the opportunity to address any such rejection.

Regarding Claims 65-67, the Examiner argues that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the data forwarding, transmitting, and receiving taught by Abraham-Fuchs to the method of Winkler for the obvious benefits taught by the former, i.e. it allows the point of care location to obtain relevant diagnostic information without resorting to the use of a centralized laboratory (Column 2, lines 26-30).

As discussed above, the teachings of Winkler are deficient, among others, in making no disclosure or suggestion of a movable aerodynamic seal. The teaching of Abraham-Fuchs, when combined with Winkler, does not overcome these deficiencies.

Conclusion

Claims 38-68 satisfy the requirements of 35 U.S.C. §§112, 102 and 103. Allowance of the above-identified patent application, it is submitted, is in order.

Respectfully submitted,

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